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Domiciliary Tuberculosis Due to Bovine Tubercle Bacilli.—Although by the end of 1933 nearly 80 cases of bovine pulmonary tuberculosis had been discovered in Great Britain, no evidence had been obtained of transmision of bovine bacilli from one human being to another, and indeed it was seldom possible to elicit a history of clinical tuberculosis in another member of the household. Walker, in 1934, reviewed the recorded instances where, in a household containing one case of bovine phthisis, others of the family suffered from tuberculosis and reported in detail the bacteriological findings in two families, in each of which the supposed contact cases proved to be of the human type. Griffith himself has reported 4 instances of domiciliary (family) nonpulmonary bovine type tuberculosis, and now, as a result of studies in 1934, adds details of two families, each of which contained 2 cases of adult pulmonary tuberculosis and one also a case of childhood lymph-node tuberculosis, all of the bovine type. *Family 1:* In April, 1934, the M. O. H. for the county of Clackmannan reported the cases of a brother and sister with pulmonary tuberculosis whose mother had been a milker and was afterwards notified (reported). Specimens of sputum from the brother and sister were found at Cambridge to contain only bovine type bacilli. The mother, born February, 1887, had 10 children between 1904 and 1924, and was first reported as having tuberculosis in June, 1916, after the birth of her seventh child. She improved under home treatment, and on several occasions tubercle bacilli were not found in the sputum. One of the children, born in 1919, had pleurisy with effusion at the right base in 1932 and a patch of apical infiltration which cleared up and is now well. The father of the children gave a negative history. The 2 children whose cases are reported were born in 1905 and 1907. The elder, a son, developed at the age of 26 right chest pain, cough and loss of weight and his case was reported in February, 1931, at which time he showed signs of pulmonary tuberculosis without cavitation. He had hospital and sanatorium treatment at intervals, with improvement, but continued to show bacillary sputum. He was fond of milk. Examination of his sputum at Cambridge in 1934 and 1935 showed short plump bacilli of the bovine type. The girl, his sister, worked in a paper-mill until marriage at 18, never milked cows, and was not particularly fond of milk. In November, 1933, at the age of 26, she developed persistent cough, loss of weight and night-sweats. On hospitalization May, 1934, she had signs of right apical cavitation, later extending to the left, and sputum was copious. She also had diarrhoea and died July, 1934. Necropsy showed extensive destruction of the left lung and upper part

of the right, with caseous pneumonia. The mesenteric lymph nodes showed calcified nodules. Pure cultures of bovine tubercle bacilli were obtained from the sputum. *Family 2:* Here there were 3 persons, man, wife and child. The wife was first observed, in July, 1933, at Glenlomond Sanatorium, where she was very ill and dyspnoeic, with signs of extensive disease of both lungs, laryngeal involvement, and chains of shotty cervical lymph nodes. The sputum contained many long, curved and beaded tubercle bacilli, with the characteristics of a dysgonic bovine strain of lower than standard virulence. The patient improved somewhat during eleven months' residence. The husband, then living in Fifeshire, Scotland, sent specimens of sputum to Glenlomond and Cambridge. They showed numerous tubercle bacilli, identical with the wife's strain. Three children, all of whom reacted to tuberculin, were examined and gastric lavage done, with guinea-pig inoculation, yielding one positive result, the bacilli being of the same type. The M. O. H. of Gillingham, Kent, obtained a very complete history of the woman's case. She was born in 1904 in a rural part of Kent and fed after the age of 9 months on cow's milk, often raw. At 4 years she had measles, followed by "bronchitis" and pleurisy with effusion, after which she was "always bronchial" but attended school fairly regularly. At 10 she was febrile and ill a month, and at 16 or 17 was anaemic and coughed. She married at 18 and had 3 children, never feeling well after the last. In 1929, pulmonary tuberculosis was diagnosed (at 25) and she spent some time at a sanatorium in Kent. Her sister also suffered from pulmonary tuberculosis in 1922, but now seems well. The husband was born at Methil, Fifeshire, in 1896, and both his mother and a sister died of pulmonary tuberculosis at home. He joined the army in 1915 (age 19), but began to cough in 1918 and in 1925 was not allowed to proceed to India on this account. He married in 1923 (at 27). He was discharged from the army with the diagnosis of pulmonary tuberculosis in 1929 (at 33), and since then lived with his family at Gillingham until transfer of the family back to Fifeshire was arranged. Here he was found to have extensive bilateral pulmonary tuberculosis with abundant sputum containing bovine type bacilli of lowered virulence. The child whose gastric washings were positive showed palpable posterior cervical lymph nodes, a suggestion of enlarged mesenteric lymph nodes, and X-ray of the chest showed bilateral root infiltration. The other children showed suggestive findings. *Summary and discussion:* The bacteriological evidence in these two families establishes that all 5 cases were of the bovine type. In the first family the mother had been a milkmaid and her own source of infection was probably alimentary as well as those of the 2 children. In the other family the facts are more complex and family infection seems more probable, since attenuated bovine bacilli in phthisis are rare (only noted in 3 out of over 120 cases of bovine pulmonary tuberculosis). The husband seems the most likely primary source.—*Family Tuberculosis Due to Bovine Tubercle Bacilli, A. S. Griffith and W. T. Munro, British M. J., July 27, 1935, no. 3890, 147.*—(*A. P.*)

Tubercle Bacilli in Sewage.—The sediment and clear effluent from hospital sewage contained spores, acid-fast filaments and acid-fast bacteria morphologically indistinguishable from tubercle bacilli. From sewage, treated initially and 24 hours later with 15 per cent sulphuric acid for 20 minutes, tubercle bacilli failed to develop or were overgrown by acid-fast saprophytes, while the viability of tubercle bacilli not mixed with sewage was unaffected by treatment with the sulphuric acid. Similarly the viability of tubercle bacilli mixed for 24 hours with the stool of a normal individual remained unaffected and the organism could be recovered from such stools after treatment with 15 per cent sulphuric acid, while in no instance were tubercle bacilli recovered after treating the stools of patients suffering from intestinal tuberculosis with sulphuric acid. As a result of these observations the authors concluded that the viability of tubercle bacilli is affected by sewage and by ferments. Subsequent studies indicated that the associated bacteria could be destroyed by treating the sewage with 5 per cent sulphuric acid for 15 minutes, including the time for centrifugation, without at the same time destroying tubercle bacilli. When such treated sewage was injected into the peritoneal cavity or into the subcutaneous tissue of guinea pigs, a more or less localized and encapsulated tuberculous process resulted, which was reinoculable into other animals. The reinoculated animals developed a more extensive generalized tuberculosis, suggesting an increase in virulence of the tubercle bacilli.—*Zum Nachweis virulenter Tuberkelbakterien in Kläranlagen, H.-G. Abshagen and A. Schinzel, Zentralbl. Bakt., July, 1935, cxxxiv, 375.*—(*J. D. A.*)

Adult-Type Tuberculosis Following Childhood Form.—In a study of tuberculosis in New Haven, of 155 children originally classified as having childhood-type

tuberculosis, 9, or 5.8 per cent, have developed the adult form. The average period between the recognition of the childhood-type and adult-type disease was 2 years and 9 months. At present there is little agreement among reports from various authors as to the frequency of progression from childhood-type to adult-type tuberculosis, and further studies are needed to enable health-officers to determine whether or not to institute extensive case-finding facilities for disease of the childhood type.—*Development of Adult Type Pulmonary Tuberculosis Following the Recognition of a Childhood Form, H. R. Edwards, Am. J. Pub. Health, August, 1935, xxv, 941.*—(*E. R. L.*)

Tubercle Bacilli in Newborn.—Cases of undoubted congenital tuberculosis are rare. It is conceivable that tuberculous involvement of the placenta may lead to haematogenous transmission of tubercle bacilli to the foetus. In one case, in fact, the authors obtained a positive blood-culture for tubercle bacilli from the cord-blood and postmortem from the heart's blood in an infant who died 3 hours postpartum of prematurity, without any morphological evidence of tuberculosis at necropsy. The mother had active tuberculosis. Tuberculosis also involved the placenta. Negative results as regards cord-blood and placentae were obtained in 14 other cases of parturient mothers with tuberculosis, none of whose offspring showed any manifestation of tuberculosis.—*Occurrence of Tubercle Bacilli in the Blood of the Umbilical Cord and in the New-born Infants of Tuberculous Mothers, M. Siegel and B. Singer, Am. J. Dis. Child., September, 1935, l, 636.*—(*M. D.*)

Early Diagnosis of Tuberculosis in Childhood.—In infants tuberculosis tends to an acute overwhelming general infection, and in children tends to involve the lymph nodes of the thorax and abdomen. Symptoms do not differ materially from those of the more common childhood infections. There may be listlessness, irritability, anorexia, digestive disturbances, irregular fever, night-sweats, cough and loss of weight. Haemoptysis is very rare. The best known physical sign is dulness over the sternum. Cough may be absent, or it may simulate whooping-cough or the bark of a hoarse puppy. It may imitate asthma. A common cause of chronic cough is bronchiectasis. In this, physical signs are more often at the base of the chest while in tuberculosis they are toward the upper part. In abdominal disease there may be colicky pains, vomiting and diarrhoea. There may be ascites and doughiness on palpation. The primary pulmonary focus is probably difficult to distinguish by X-ray unless calcification has occurred. Calcium infiltration is the sole distinctive radiographic indication of the site of a lymph node situated within the limits of the mediastinum and that demonstration of enlargement is rare unless calcification has occurred. Epituberculosis usually affects the right upper lobe but it may be in any part. Adult-type tuberculosis is sometimes found. Injection of lipiodol may be used with caution to differentiate bronchiectasis. In children or infants the stools and stomach contents should be repeatedly searched for tubercle bacilli. The tuberculin test tells whether the patient has had tuberculous infection but gives no information as to activity. A negative tuberculin reaction may be obtained in grave acute tuberculous conditions, acute pneumonia, measles, whopping-cough, enteric fever and influenza. Both the negative and positive reactions are of value in diagnosis. Blood examinations apparently offer little practical help.—*Early Diagnosis of Tuberculosis in Infancy and Childhood, B. Morgan, J. State Med., June, 1935, xliii, 343.*—(*L. F. B.*)

Pulmonary Tuberculosis in Childhood.—A series of 84 consecutive cases is reported by the Clinical Tuberculosis Officer, County Borough of Sunderland, England, seen at the Tuberculosis Dispensary over two and a half years, of whom 41 per cent females and 20 per cent males were found sputum-positive. In 28.5 per cent there was contact with a known case of pulmonary tuberculosis in the same household. Cough was by far the commonest initial symptom. Four groups are differentiated: *1: Fibrocaseous tuberculosis:* 41 cases, approximating the adult type and running a chronic course. Of these, 16 died, 13 are institutionalized, 9 stationary but not arrested, one quiescent, and 2 lost sight of. *2: Infiltrating type:* 22 cases, subdivided into (a) acute advancing and (b) more chronic and favorable types. Of this group, 9 died, all in the first subgroup, 3 were institutionalized, 4 quiescent, and 6 not arrested. *3: Pleurisy with effusion:* 17 cases, confirmed by X-ray and exploratory puncture and cytology. Only one death occurred, 9 are quiescent, 5 improved, one institutionalized and one lost sight of. *4: Hilar tuberculosis:* Only 4 cases, 2 quiescent and 2 improving. *Complications:* There were 7 with abdominal tuberculosis, 2 of cervical adenitis, 2 of meningitis, 3 nontuberculous. *Treatment:* In 81 cases institutional treatment was given and 4 domiciliary. *Circumstances:* Sleeping accommodations and income were both

inadequate in nearly all.—*A Series of Eighty-Four Cases of Pulmonary Tuberculosis in Children Aged 6–15 years, J. R. Beal, Tubercle, July, 1935, xvi, 452.*—(*A. P.*)

Renal Tuberculosis in Childhood.—*Frequency:* Apart from miliary tuberculosis, it is among the rarer manifestations, especially under the age of 10, but no age is exempt. Miliary renal tuberculosis, on the other hand, is a frequent necropsy finding in children dying of meningitis or general tuberculosis. In 1934, out of 14 such necropsies at the Hospital for Sick Children, Great Ormond Street, 9 showed miliary tubercles in the kidneys. The frequency of tuberculous disease of the kidney had doubtless been under-estimated in the past, and there is no doubt that in association with other active haematogenous lesions (for instance, spine and hip), it is not so rare. But in the early stages there are no urinary symptoms, and the pyuria is so slight and intermittent that it escapes notice unless careful microscopic examinations of the urine are made. Harris, at the Hospital for Sick Children, Toronto, found that 9 out of 67 children (13.8 per cent) with bone tuberculosis had tubercle bacilluria, discovered by routine injection of urine every two months into guinea pigs. Before this, only one case had been found among 392 patients. During the last year, Addison has seen 10 cases in children, 7 with active lesions, usually of spine or hip. *Pathology:* The presence of a pyuria, even if microscopic, in association with tubercle bacilluria, may be taken as proof of a renal lesion. Experimental evidence is against the filtration theory (Medlar), and Helmholtz showed that organisms are not found in the urine without renal lesions. Band, in a recent study, isolated from 174 cases of extraurinary tuberculosis 25 (14.4 per cent) with tubercle bacilluria by animal inoculation. Young's dictum that the original infection is practically always confined to one kidney is untenable in view of the fact that renal tuberculosis is haematogenous in origin. Although macroscopic appearances of actively advancing lesions indicate more advanced destruction in the medullary than the cortical zone, the cases examined microscopically by Medlar and by Band showed mainly cortical lesions, arising usually in a glomerulus or a capillary between two adjacent tubules. Usually, wedge-shaped abscesses form in the medulla with their apices in the pyramids. If the disease progresses the ureter sooner or later becomes involved, tubercles form in the mucosa and coalesce into ulcers. Blocking of a ureter by granulation and fibrous tissue is not uncommon. The bladder becomes involved by the passage of tuberculous urine, the region of the ureteral orifice being first affected. *Symptoms:* In the earliest stages there are no symptoms, but only a slight pyuria. Haematuria is nearly always the first objective sign, usually slight and tending to recur at intervals, with increasing pyruia. Until the disease is well advanced, contamination of the urine is not noted and at first the general health is unaffected. Later, with increasing pyuria and frequency, come a little irregular pyrexia but for considerable periods the temperature may remain normal. When the kidney becomes disorganized, an irregular temperature, with nocturnal rise, is the rule. Pain is not marked in the absence of complications. Increased frequency of urination follows involvement of the bladder. Pain may be absent even with the bladder capacity reduced to an ounce or less. *Diagnosis:* This is established by the discovery of the tubercle bacillus, which should be carefully sought for in every case of unexplained chronic or intermittent pyuria. If necessary, a twenty-four-hour specimen should be collected and centrifugated and, if negative on examination, the residue should be injected into a guinea pig. X-ray examination may show increased renal density or calcareous areas when disorganization has occurred, and an intravenous pyelogram irregularity of the pelvis and destruction of the calices. As there are difficulties in getting good pictures by this method the ureteral method may be substituted and is not dangerous except perhaps in early cases. Cystoscopy is always necessary. A little redness and swelling around one ureter, followed by inflammation of the trigone and tubercles and ulceration at the base of the bladder, are the usual sequence. *Course, prognosis and treatment:* Once the disease is well advanced, arrest is unlikely although attempts at repair are common, evidenced by areas of fibrosis and calcification. In the early stages, the child should have sanatorium treatment and preferably be in bed. Pyelograms are of limited value in early diagnosis and, if done, should be by the intravenous method. The urine must be examined microscopically at regular intervals and the number of organisms and pus cells estimated. When the disease is advanced and unassociated with other active lesions nephrectomy should be done if renal function is good and no tubercle bacilli are found on catheterizing the other ureter. Even with involvement of the other kidney, if slight, nephrectomy may be well worth while. When there are active foci in the spine, other bones, etc., the general condition must be

carefully considered. But it is surprising how rapidly a tuberculous bladder may heal and tubercle bacilli vanish from the urine once the damaged kidney is removed.—*Tuberculosis of the Kidney in Childhood, O. L. Addison, British M. J., September 28, 1935, no. 3899, 565.*—(*A. P.*)

Open Pulmonary Tuberculosis in Children.—The case-records of 710 children discharged from High Wood Hospital, Essex, England, between 1922 and 1931, inclusive, comprised those of 470 girls and 240 boys. Their ages ranged from 3 to 15 years, and all were sputum-positive, except a small group with positive faeces. They are subdivided into groups according to their clinical course: *1: Cases following a chronic course:* This was the largest group, including 35 per cent of the girls and 39 per cent of the boys. The period of survival from the time of admission to death ranged from two to ten years. To this, however, is added 2 subgroups: *A: Apyretic but with rapid pulse:* This group includes an additional 6 per cent of the girls and 5 per cent of the boys. They were constantly afebrile, but the evening pulse was consistently high and they failed to gain weight. *B: Febrile but gaining weight:* This group includes an additional 4 per cent of the girls and 3 per cent of the boys. Despite evident toxaemia, they were happy and had a good appetite, resenting confinement to bed. Thus, the sum total of the chronic groups was represented by 45 per cent of the girls and 47 per cent of the boys. *2: Cases following an acute course:* This group consisted of 23 per cent of the girls and 13 per cent of the boys. The picture was typical of acute phthisis with marked toxaemia, and necropsy findings showed tuberculous bronchopneumonia. This type was most common in girls of 14 and 15, and terminated fatally in one to nine months. To it is also added *A: A subacute group*, surviving somewhat longer and including 3 per cent of girls and 8 per cent of boys. *3: Cases completely or partially recovered:* This group included 17 per cent of the girls and 21 per cent of the boys. No points were revealed which might be taken as prognostic indications. Some had extensive involvement. *4: Cases initially improved followed by rapid decline:* This group included 5 per cent of the girls and 3 per cent of the boys. *5: Unclassified group:* This group either had but a brief stay, terminated in some fatal complication, or could not be satisfactorily grouped. In some cases rapid deterioration followed haemoptysis. It included 2 per cent of the girls and 8 per cent of the boys. *Complications:* In a certain proportion the course of the disease is too rapid for extrapulmonary complications to be observed but in many others they may be noted if sought for: *1: Haemoptysis:* Frank haemoptysis was noted in 22 per cent of girls and 25 per cent of boys. It is especially terrifying to children. *2: Laryngitis:* This, as Agassiz has shown in Great Britain and Armand-Delille and Caboche in France, is far more common than has formerly been supposed. Gravesen and Godbey now urge monthly largyngoscopic examination in both children and adults. *3: Spontaneous pneumothorax:* Of 117 deaths in the hospital 15 per cent were due to this cause. In all, 24 cases were recorded, 14 in girls, and in nearly all death ensued. *4: Fistula-in-ano.* This was noted in 7 boys and 2 girls. *5: Enteritis:* This undoubtedly occurred oftener than recorded. It was common in advanced cases and of bad prognostic omen. *Remarks, prognosis and results:* Pulse-rate and weight are more accurate indices than the temperature. The ability to gain weight is important evidence of improvement in the absence of obvious increase in the lesion. Weekly weight-records are essential and also records of pulse-range, provided proper precautions are observed with the latter. The gravity of prognosis of pulmonary tuberculosis in children has been frequently set forth. Girls especially show an extremely high death-rate. In this series the mean duration of illness in girls was 23.8 months and in boys 29.6 months, the median 18.4 months and 24.2 months, the mode 7.6 months and 13.4 months. At puberty especially a rapid spread and fatality occurs among girls. But girls who menstruate regularly show a lower death-rate than those in whom the menses are interrupted.—*Course, Complications and Prognosis of Open Pulmonary Tuberculosis in Children, E. Cochrane, Tubercle, September, 1935, xvi, 529.*—(*A. P.*)

Monocyte-Lymphocyte Ratio in Children.—The relation of monocytes to lymphocytes (M:L) in the peripheral blood of tuberculous individuals has been studied with respect to the clinical status of the disease and the reaction to the injection of tuberculin. In children that reacted positively to the Mantoux test, a large majority (84.2 per cent) exhibited an increase in the M:L ratio, which was usually at its height in 48 to 72 hours. The average change was from a ratio of from 0.13 before the tuberculin test to 0.35. In one case the ratio increased to 0.81. In the small number of controls (children with negative tuberculin reactions) the change in M:L following the application of the test was comparatively insignificant.—*Effect of Tuberculin Test on*

Monocyte-Lymphocyte Ratio in Children, K. Kato, Jour. Ped., August, 1935, vii, 238.—(M. D.)

Declining Tuberculosis Death-Rate in Children.—In Minnesota all deaths from tuberculosis occurring in children under 15 years of age for the 18-year period 1915–1932, were tabulated. The deaths for each of these years were divided into 7 groups: under 1 year; 1 to 2 years; 2 to 3 years; 3 to 4 years; 4 to 5 years; 5 to 10 years; and 10 to 15 years. These statistics show that in Minnesota tuberculosis mortality rates in children are lower and have decreased at a more rapid rate than those reported by Wallgren in Gothenburg, Sweden, with the use of *BCG* vaccine. There were 2,946 deaths from all forms of tuberculosis reported in children under 15 years of age. In 1915, 32 per cent of the tuberculosis deaths under 15 years occurred in the group under one year, while in 1932 only 14.5 per cent of the total deaths were in this group. Although the mortality rate under 1 year has decreased more than 80 per cent during this 18-year period, the death-rate remains higher for the group under 1 year than for any of the other groups under 15 years. Between 1915–1917 and 1930–1932 the mortality from tuberculosis declined 72 per cent for all children under 15 years of age, 88 per cent for infants under 1 year, and 58 per cent for the general population in Minnesota. Between 1915–1920 and 1921–1926 there was a decrease of 37.5 per cent in the tuberculosis mortality in children, and between 1921–1926 and 1927–1932 a reduction of 35.9 per cent. The types of tuberculosis causing the greatest number of deaths in children in the order of their importance were tuberculous meningitis, pulmonary tuberculosis and miliary tuberculosis. The largest percentage of deaths from tuberculous meningitis occurred in children under 5 years of age and from pulmonary tuberculosis in those between 10 and 15 years of age. Lymph-node and bone-and-joint tuberculosis are negligible as a cause of death in children under 15 years of age.—*The Declining Death Rate from Tuberculosis in Children. An Analysis of Tuberculosis Deaths in Minnesota from 1915 to 1932, Ruth E. Boynton, J. Am. M. Ass., May 25, 1935, civ, 1875.—(G. L. L.)*

Avian Tuberculosis in Swine and Cattle.—Swine tuberculosis in Wisconsin decreased some 11 per cent from 1922 to 1932, but increased slightly from 1932 to 1934. The general trend throughout the United States was an increase of 14 per cent from 1907 to 1924. In the Corn Belt States only has there been a gradual decrease of about 4 per cent between 1922 and 1932. Since both avian and bovine tubercle bacilli infect the hog, the earlier increase may presumably be due to an increase in tuberculosis in poultry, and the later decrease in the Corn Belt to a better control of bovine tuberculosis. Wisconsin became a modified accredited area for bovine tuberculosis in January, 1932, but inspection of the flocks of fowls showed, in 1934, approximately one-third of them to be infected. A study was made to determine, by culture and animal inoculation, the type of tubercle bacilli responsible for lymph-node tuberculosis in swine. Over 99 per cent of the tuberculosis in hogs is localized in the lymph nodes. Cultures of *Mycobacteria* were isolated from 39 of 61 lymph-node specimens examined and two cultures of acid-fast organisms were obtained from the spleens of rabbits inoculated with tissue when the lymph-node cultures were negative. Five of these 40 cultures were injected into rabbits and guinea pigs. After 5 months none of the latter showed visible tuberculous lesions. All the rabbits died within three weeks with the Yersin type of disease. One culture was smooth, butyrous, showed no tendency to form pigment, and grew a little more rapidly then the avian tubercle bacillus. By inoculation, it was nonpathogenic for guinea pigs, rabbits or chickens. Of the group from which cultures were grown, tuberculosis was produced in rabbits by only 8 of the 21 hog lymph nodes injected. These negative inoculation results can be reconciled with the positive cultural results by assuming that the tissue injected contained no tubercle bacilli. The study revealed that, when positive results were obtained, the avian tubercle bacillus was the aetiological agent in all but one case. Three of 31 specimens passed by the inspectors as normal were found to be infected by acid-fast organisms having the cultural characteristics of the avian tubercle bacillus. Cultures of an orange-pink diphtheroid were isolated from 21 of the 61 tuberculous lymph nodes, but none from the normal lymph nodes. The presence of avian tubercle bacilli in swine is important from the standpoint of public health and is in itself of major economic importance. The avian tubercle bacillus as the cause of human disease has been reported by several European workers. Under natural conditions this bacillus never gives rise to a progressive tuberculosis in the hog, but will multiply, cause but little tissue destruction and may be eliminated. Thus the hog may be considered a reservoir for maintaining the vitality of the avian tubercle bacillus and may be the source of infection

for other hogs, for chickens and for cattle.—*The Relation of the Avian Tubercle Bacillus to Tuberculosis in Swine and Incidentally in Cattle, Janet McCarter, B. A. Beach and E. G. Hastings, Jour. Amer. Vet Med. Assn., lxxxvi, February, 1935, 168.*—(*L. F. B.*)

Recovery from Johne's Disease.—Johne's disease or paratuberculosis of cattle is slowly spreading among American cattle and is more than ordinarily insidious because of its variable incubation period, symptoms that may be attributed to other causes and lesions that are not striking and are easily overlooked. In November, 1926, three heifers were drenched with infectious material. One developed symptoms at 10 months and died 13 months after infection. The second developed symptoms at 23 months and died 25 months after infection. The third showed no evidence of disease during the first year. Allergic tests were positive nearly 6 months before complement-fixation, but fixation remained positive during a long period when allergic tests were inconclusive or negative. The third animal, 21 months after infection and 6 weeks after normal calving, developed symptoms of the disease which persisted several months. Four weeks after second calving, in 1929, symptoms returned. Following improvement and the disappearance of symptoms there was no further evidence of disease during her life. A section of ileum removed in 1935 showed no evidence of disease. Complement-fixation tests were positive but allergic tests were inconclusive. No organisms were found in the faeces. The animal was slaughtered at 9 years of age, eight and one-fourth years after infection and 5 years after evidence of disease had disappeared. Calcareous plaques in the common aorta and pulmonary artery, near the valves, were present. This lesion is rather common. A 10-cm. pelvic abscess was found. In the intestine nothing was found except a large thickened, congested and folded area in the caecum. Smears of mesenteric lymph nodes and those near the caecum showed typical acid-fast bacilli. Sections of the caecal patch showed a fairly marked, typical lesion. When the disease was at its worst the lesions were undoubtedly much more extensive and widespread throughout the intestine, and it is remarkable that the characteristic proliferations could be absorbed so completely. It is reasonable to think that animals may completely recover from Johne's disease. If an advanced case may occasionally recover it is more likely that animals may often contract infections from which they may recover without reaching the advanced stage in which symptoms are produced.—*Recovery from Johne's Disease, W. A. Hagan and A. Zeissig, J. Am. Vet. Med. Assn., August, 1935, lxxxvii, 199.*—(*L. F. B.*)

Rat Leprosy.—When the new freezing and drying technique of Gersh was used before the Ziehl-Neelsen stain on sections of tissues containing rat leprosy bacilli or human tubercle bacilli, the bacilli were distinctly less granular than in sections of the same tissues preserved by the usual methods, that is, in 10 per cent formalin in absolute alcohol, or Regaud's fluid, or in straight 10 per cent formalin or formalin-Zenker's in the case of the tubercle bacilli. These observations suggest that there is some unsuspected flaw in the freezing and drying method, or that the bacillus of rat leprosy and the human tubercle bacillus, as they exist in the tissues, are less granular than is commonly supposed.—*Morphology of Bacillus of Rat Leprosy, E. V. Cowdry and L. F. Heimburger, Proc. Soc. Exper. Biol. & Med., June, 1935, xxxii, 1422.*—(*F. B. S.*)

Pathogenesis of Tuberculosis.—At the present time, many and possibly the majority of physicians favor the opinion that a tuberculous infection confers a degree of protective immunity on the patient which operates to diminish afterward the chances of serious forms of tuberculosis developing. According to this view, when equal average chances for infection by uncontrolled contact exist per group, the infected tuberculin-sensitive portion of the population is expected to withstand reinfection with greater success than that with which the remaining nonallergic, presumably unprotected part resists accidental primary infection. As a matter of fact, the opposite point of view is more reasonable, namely, that first infections are usually withstood well, provided that miliary tuberculosis or tuberculous meningitis does not occur; whereas, reinfection in previously sensitized persons is most apt to produce phthisis of extensive and serious degree. This conclusion is based in large part on the statistical analysis of the records of the 11,000 children studied at the Lymanhurst School since 1922, of whom about two-thirds had negative tuberculin reactions when first seen. Of the entire group, 2,049 children could be studied quite thoroughly over periods ranging from one to twelve years. In the study of the data, the factors of social status and degree of exposure to infectious surroundings were considered. The conclusion drawn was that initial infection with tuberculosis, aside from

the danger of resulting miliary dissemination or meningitis, leads to a change in tissue sensitivity which is distinctly harmful as regards later reinfection, whether of exogenous origin, or of endogenous source from foci established at the time of first infection. Even though the first infection is massive and may result in very extensive pulmonic infiltration, it is usually well handled and does not exhibit the totally distinct and unlike picture of reinfection phthisis with its tendency to spread, to cavitate, and to cause symptoms. Caution probably should be exercised in advancing a positive unqualified view that a first infection with tubercle bacilli is a beneficial protective experience. The tested safe method by which tuberculosis can be prevented is by retaining the normal uncontaminated state of the tissues, a condition which operates to prevent more than 99 per cent of all initial infections acquired in the first fifteen years of life from producing fatal forms of tuberculosis during this period.—*Pathogenesis of Tuberculosis in Man: Certain Governing Principles and the Causal Relationship Existing Between Primary and Reinfection Types of the Disease, C. A. Stewart, Am. J. Dis. Child., October, 1935, l, 853.*—(*M. D.*)

Monistic Nature of Tuberculous Lesions.—A unitary concept of the pathology of tuberculous lesions is desirable and necessary for a clear understanding of the disease. The alternative dualistic concept was championed by Virchow. It is reiterated that microscopic and macroscopic studies of tuberculous lesions lead to the conclusion that the histogenesis of tuberculous processes partakes of the nature of all inflammations. Tissue destruction, disturbances of circulation, exudation, granulation-tissue formation, and cicatrization, occur in tuberculous processes exactly as they do in other inflammations. The characteristic features of tuberculous processes—caseous necrosis in exudative states and epithelioid giant-cell formations in productive states—are a reflection of the specific characteristics of the tubercle bacillus. The variations in histological formations in different organs are functions of the variations in tissue structure. Those who accept this unitary concept only with reservations, and those who do not accept it at all, usually fall back on Baumgarten's classical experiments—the occurrence of nodular tubercles in the anterior chamber of the eye as the primary sequence of the injection of tubercle bacilli—to sustain their point of view. For this reason Baumgarten's experiment was repeated. Various doses of bovine tubercle bacilli were injected into the anterior chambers of the eyes of 6 rabbits. These animals were killed at periods ranging from 24 hours to 3 weeks after the injection. The first thing noted in these animals was a severe acute inflammation of the eyes with a more or less definite hypopyon. This inflammation subsequently receded. This finding was fully confirmed by microscopic study. The earliest response to the presence of tubercle bacilli in the anterior chamber of the eye was shown to be a simple inflammation. Subsequently there developed, in this inflammatory area, typical tuberculous granulation tissue and giant-cell tubercles. In other words, Baumgarten's results were verified, but were shown to represent the end-stage rather than the beginning of the process. The specific organization of the initial nonspecific inflammation took place some time between the 3rd and 10th days following the injection. The histological changes in the anterior chamber of the eye of the rabbit, following the injection of tubercle bacilli, therefore furnishes further evidence for a unitary concept of the development of tuberculous processes, namely, an exudative state with more or less pronounced caseous necrosis, followed by a productive state with the formation of epithelioid-cell tubercles.—*Bemerkungen zu einigen Grundfragen der menschlichen Tuberkulose, P. Huebschmann, Schw. med. Wchnschr., March, 1935, lxv, 289.*—(*A. E. M.*)

Tuberculosis as Organ-System Disease.—From a study of a group of cases of multiple tuberculosis of the greater circulation, it appears that the infection has the tendency to locate in one organ-system and to leave the remaining organs unharmed. For example, the disease usually appeared as extensive joint and bone tuberculosis, or as skin or urogenital tuberculosis, and not a mixed infection of all these organs, as one might expect. This phenomenon is explained on the basis that the susceptibility of different tissues to infection varies from case to case. Among 371 cases of tuberculosis, 22 to 33 per cent had the infection localized in the lungs or cervical lymph nodes. About half of these were really serious forms of tuberculosis, consisting almost exclusively of solitary or multiple haematogenous infection in the greater circulation. Half of the multiple haematogenous infections began as mild forms of tuberculosis, whereas only 10 per cent of the solitary infections began in this manner. Haematogenous infection in an organ of the greater circulation appeared secondarily to a severe typical phthisis in only about 3.5 per cent of the cases. Haematogenous infection occurred in nearly half of the patients (176) as multiple, and in the

remainder (196) as solitary lesions. The solitary lesions were localized in the joints and bones. Of all cases studied, by far the greatest number showed localization in the bones and joints. Since all the organs of the greater circulation must be exposed equally to infection there must be a special susceptibility of the bone-and-joint system for the tuberculous infection in these patients. Patients with bone or joint tuberculosis seldom have skin or urogenital lesions, and *vice versa*. This rule for the relationship between the affinity of various organ systems for tuberculosis holds true also for lung tuberculosis, for only 24 typical phthisis cases were observed among 371 patients with bone-and-joint tuberculosis. In short, chronic tuberculosis seems to localize itself in one organ system, often as a multiple infection, leaving the other organs unharmed. It seems to be an organ-system disease. The pathogenesis of tuberculosis is discussed. Usually when tubercle bacilli enter the body they are deposited as latent foci. Later, due to some trauma, there arises a local lowering of tissue resistance and consequently a significant focus follows. Similar kinds of tissue develop a sensitivity to the infection and when a renewed haematogenous inoculation of tubercle bacilli occurs, these sensitive tissues develop foci and there follows an organ-system disease.—*Tuberkulose als Organsystemerkrankung. (Ein Beitrag zur Klinik und Pathogenese der chronischen Tuberkulose), J. Meyer, Acta Tuberc. Scandinav., Fasc. 2–3, 1935, ix, 67.*—(*F. B. S.*)

Note: Not a few of the above statements are so against ordinary clinical experience as to attract attention, yet surely require little, if any, critical comment.—*A. K. K.*

Initial Lobar Tuberculosis.—From its incipiency pulmonary tuberculosis may be lobar in type. The roentgenogram reveals an opacity occupying all or a major part of the lobe (most often the right upper) with the interlobar fissure making a sharp delineation. Lateral views give additional evidence of its limitation to one lobe. Usually the density is greatest in the region directly above the fissure, so that at certain stages of the pneumonia the apex may be translucent. Frequent X-rays are necessary, since at the onset there are no clinical or roentgenological guides to indicate which of the following courses the lesion will take. *1:* As in an infraclavicular lesion, the lobar infiltrate may absorb completely within several months and leave practically no trace, or, at most, fibrotic infiltrations or a thickened interlobar fissure. *2:* The acute state may subside and the tuberculous process become fibroulcerative. *3:* Early cavitation and bilateralization may take place at any time. When a single cavity forms, it will most likely be just above the fissure. Occasionally the disease in the rest of the lobe clears simultaneously, leaving a cavity which has a configuration and position not unlike the cavity which may arise from an infraclavicular infiltrate. *4:* The malignant type of lobar tuberculosis evolves as a caseous lesion and rapidly goes on to cavity-formation. In rare instances (2 out of 800 autopsies) the patient succumbs before ulceration takes place. In retrospect, some patients recall that for a variable time preceding the acute episode they had the "grippe" or "influenza." The acute onset, or exacerbation, of the disease was accompanied by one or a combination of the following symptoms: high fever, chill, chest pain, haemorrhage. Less often the X-ray features of lobar consolidation are found in patients who present a paucity of symptoms, and these mainly catarrhal, whose time of onset is rather indefinite but of comparatively recent date. In some instances the serial roentgenograms reveal the lobar consolidation to be an intermediary stage or an end-result of an at one time extensive bilateral pulmonary tuberculosis. On physical examination initial lobar tuberculosis may reveal few, if any, abnormal changes or else classical signs of consolidation. The latter is more likely in malignant lobar tuberculosis. Treatment is often delayed because of incorrect diagnosis. At times the condition may be confused with lobar pneumonia, pulmonary neoplasm or suppuration, or interlobar effusion (rarely). Tubercle bacilli may not be found until late in the disease, if ever. The latter is particularly true in adults with benign lobar tuberculosis and in children. Pneumothorax is often necessary and is employed early in the course of the disease. Usually a free pleural space is found and the collapse is so selective an associated atelectasis of the diseased lobe is suggested. When the disease is symptomatically benign, the pneumothorax can be withheld while the course of the disease is very carefully watched. The importance of frequent roentgenograms cannot be overestimated.—*Initial Lobar Tuberculosis, E. H. Rubin, Am. J. Roentgenol., August, 1935, xxxiv, 175.*—(*E. M. J.*)

Note: The long recognized and described *phthisis florida* is, of course, the exemplar of the above condition. Contrary to common opinion, phthisis florida is excessively rare. Characteristically, of from one to three months' duration (after hospital admission) and inevitably fatal, it may be impossible of

absolute diagnosis (lack of demonstrable tubercle bacilli) before autopsy. The usually accepted cause (there are others) is the massive discharge of caseating, liquefying lymph nodes from pulmonic root to one or both lungs. Because the disease (especially autopsy) can be so spectacular, it is prone to leave an indelible impression on the observer. A characteristic case was described by Heise and Krause in an issue of THE AMERICAN REVIEW OF TUBERCULOSIS, some fifteen years or so ago. With sputum tubercle-negative after eight or nine weeks of daily examination, the diagnosis remained doubtful, (cancer was considered) until a positive specimen turned up. Death ensued from haemopneumothorax, suffered immediately upon a first attempt to induce therapeutic pneumothorax. The cause of the accident was *not* needle-puncture of the lung, but the breaking of a thinned-out pleura, overlying a cavity and made taut by a single stout, short adhesion.—*A. K. K.*

Productive Lesions in Tuberculosis.—Five hundred cases of tuberculosis are reviewed mainly because of the marked changes which have occurred in the method of treatment during the past few years, especially in the use of surgical procedures. This type of treatment is in marked contrast to the prolonged periods of bed-rest formerly employed, with little promise to the patient of a real cure. The cases studied were the first 500 having a predominantly productive lesion which were found by reviewing X-rays of patients entering Herman Kiefer Hospital in the years 1930 to 1934. The productive lesion was chosen because of its chronicity and difficulty in treating. Those having this type of lesion comprised 23.2 per cent of all tuberculous patients admitted in the four-year period. There were twice as many males as females in this group. The proportion of Negroes was about the same as the proportion in the hospital at the present time and no difference could be discovered in their response to treatment. The tables presented of the minimal cases, 98 in all, show that most of the unilateral cases can be treated satisfactorily with bed-rest, that a period of bed-rest is frequently needed in bilateral cases before deciding on further treatment, and that phrenic-nerve interruption gives satisfactory results in the majority of those needing further therapy. Only one case in the minimal group needed a combination of pneumothorax and phrenicectomy, and only one case passed out of control. Of the 142 moderately advanced cases, approximately one-third had unilateral lesions. Rest in bed was useful only in one-fourth of these patients, but in a larger number of the bilateral cases bed-rest was the most suitable treatment. Phrenic interruption was adequate in controlling one-half of the unilateral lesions, and only one-eighth of this group needed a combination of phrenic interruption and pneumothorax. Phrenic-nerve crushing alone will frequently close cavities in unilateral lesions, so that this is usually done first and other therapy added later if necessary. Cases with negative sputum, but showing cavities, were treated just as vigorously as those with similar findings and a positive sputum. The bilateral cases presented a more difficult problem because of the frequency of cavitation, complications and poor physical condition. An attempt is made to close cavities in all cases and render the sputum negative. Frequently this is done by instituting pneumothorax on the worst side and performing a phrenic crushing on the opposite side. For cases of bilateral cavitation, bilateral pneumothorax was given and not infrequently phrenic crushing was added to the side slowest to respond to the pneumothorax. The productive lesions are frequently neglected, no treatment being sought until the patient is incapacitated. Many patients, therefore, are in the far-advanced group. In this series a little over one-half were far-advanced cases. They presented serious problems. Eight of the unilateral cases and over one-half of the bilateral cases were unfit for anything but bed-rest and symptomatic treatment. Many of them also had extrapulmonary lesions. The extrapulmonary lesion frequently subsides if the pulmonary disease can be controlled. Everything was done to close cavities, but in many this was impossible. A surprisingly high incidence of tuberculosis was found among food-handlers, making it easy to understand why many other patients do not know the source of their infection. The diabetic showed very little difference from nondiabetic patients in their response to treatment. The author concludes from the data presented that a chronic case of tuberculosis will respond as well to collapse therapy as any other type, few complications actually contraindicating therapy.—*The Management of the Productive Lesion in Pulmonary Tuberculosis, C. C. Birkelo and S. M. Gilenger, Radiology, January, 1925, xxiv, 58.*—(*G. F. M.*)

Monocytes as Source of Alveolar Phagocytes.—The primary source of the alveolar phagocytes of the lung has long been a matter of debate. No method has been unassailably successful in marking the suspected progenitor of the alveolar phagocyte in such a fashion that its progress from

the source of supply to its position as a free cell in the alveolar spaces could definitely be followed. In the present article a method is described which eliminates this obstacle by obtaining marked viable monocytes from one animal, injecting them into the circulation of a second animal, and observing the behavior and distribution of the transferred cells in the new host. If the marked cells later appeared as alveolar phagocytes, support would be obtained for the belief that circulating monocytes may become alveolar phagocytes. The procedure was as follows: *1:* A suspension of leucocytes (monocytes) was obtained by the production of a chemical peritonitis in guinea pigs by the intraperitoneal injection of aleuronat and starch. *2:* The cells were marked by a method of phagocytosis of suspensoid dyes *in vivo*. India-ink and carmine were the marking materials, the former being used in the majority of the experiments. The suspension of marked cells was then removed, cleared of free pigment by filtering through paper, washed and standardized so that each cmm. contained 50,000 cells. *3:* The viability of the cells thus obtained was established by phagocytic tests *in vitro* utilizing a contrasting pigment. Over 50 per cent of the marked cells were found to be viable. *4:* The standardized marked viable suspension was injected into homologous animals (other guinea pigs) at various points of their circulation. Animals free from anthracosis were purposely selected for the experiment. A control group received a pure suspension of india-ink in physiological saline solution. *5:* The recipient animals were killed at various times, sections of the lungs and other organs made, and the distribution of the marked cells noted. *Results:* The dye-containing cells were found almost entirely in the lung tissue. Some were seen within the pulmonary capillaries, some appeared in the lung stroma, but the vast majority were found to be either free in the alveolar spaces or applied to the alveolar walls, apparently lining the walls and thereby presenting the morphological picture of alveolar epithelium. In several instances pigment-bearing mononuclears were seen escaping from pulmonary capillaries. The liver, spleen and bone-marrow contained occasional dye particles obtained from disrupted nonviable marked cells. The criticism that the injected cells are destroyed in the blood-stream of the recipient animals and the liberated pigment then phagocytosed by certain cells residing in the pulmonary parenchyma is refuted by the fact that suspensoids have no power of diffusion. When a solution of india-ink was injected, none of it was ever found in the alveolar spaces or in the cells lining their walls. Alveolar phagocytes are derived largely, if not entirely, from the monocytes of the circulating blood.—*Monocytes as a Source of Alveolar Phagocytes, J. Ungar, Jr., and G. R. Wilson, Am. J. Path., July, 1935, xi, 681.*—(*J. S. W.*)

Mechanical Production of Cavities in Isolated Lungs.—A method is described by which defects simulating smooth-walled, round cavities, bronchiectasis, emphysematous bullae, and cystic disease of the lung may be produced mechanically in the isolated lung. By means of bronchoscopic punch forceps introduced through the bronchi of isolated, unopened human and calf lungs, it was possible to produce mechanical laceration, rupture of the bronchial walls and surrounding lung tissue and to remove various amounts of tissue so as to produce gross defects. Roentgenograms and sections were then made before and after inflation. The size of the cavities was found to be disproportionate to the degree of laceration or loss of lung substance but depended principally on the amount of pressure during inflation. In cases in which simple lacerations along the bronchial wall had been made, the cavities were elongated, slightly tortuous tunnels with slightly scalloped surfaces and narrow ridges simulating closely the appearance of bronchiectasis and often ending in larger spherical cavities. Where a measurable amount of lung tissue had been chewed out, a balloon-like cavity of large size was produced with a smooth, rounded inner surface except for a number of ridges, or thin, tightly stretched bands of fibrous tissue or vessels. A definite wall was formed about the cavity by a narrow zone of collapsed lung tissue, visualized in the roentgenograms as a definite, thin, annular shadow. When the original defect was close to the pleura, a more pronounced bulging of the surface of the lung at this point during inflation was noted and the greatest stretching took place in this region. As long as expansion of the lung was maintained the large round cavity was also maintained, but, when the lung was allowed to deflate, the cavity decreased proportionately. However, the cavity never returned to its original size and shape unless the lung was deflated by suction. Occasionally a cavity was created by inflation which withstood every effort to collapse it by suction, or positive pressure outside the lung, and cross-sections made through the cavity revealed that it had been formed within one of the larger, interlobular septums and sealed off from the bronchi as if by a valvular

flap. The walls of many cavities were examined microscopically and revealed a narrow zone of completely collapsed lung tissue in which alveoli, connective-tissue septa and the flaring openings of small bronchi were found. In the mechanical production of pulmonary cavities two factors are necessary; one is the laceration of the fibroelastic framework of the lung in order to produce an area of abnormal yielding to stretching by inflation; the other is the inflation of the lung by which lacerations and defects assume a rounded shape as they expand, according to the laws of transmission of pressure by fluids. Regardless of the direction or extent of laceration or the shape of the defect produced by the forcible mechanical removal of pulmonary tissue, inflation invariably results in the formation of one or more smooth-walled, rounded cavities. These experiments suggest that cystic disease, bullous emphysema, saccular bronchiectasis and the cavities of tuberculosis or abscess of the lung are products of the same mechanical factors and differ only in degree and distribution.—*Mechanical Production of Cavities in Isolated Lungs, S. E. Moolten, Arch. Path., June, 1935, xix, 825.—(A. M. S.)*

Intrapleural Pressures.—Paradoxical pleural pressures and paradoxical diaphragmatic response are not synonymous, do not occur simultaneously, and have an entirely divergent pathogenicity. Paradoxical pleural pressures were observed in 4 of 600 cases of pneumothorax. All were incomplete collapses and under positive pressure, with the pleural limiting membrane showing a convexity toward the mediastinum. Inspiration, with its attending rise of the ribs and descent of the diaphragm, tends to overcome this convexity, making the pneumothorax pocket smaller and thus giving a more positive pressure. On expiration with relaxation of the pleural membrane the pressures are less positive. Paradoxical diaphragmatic motion in pneumothorax has two explanations: *1:* When the diaphragm is paralyzed, it follows the labile mediastinum by being aspirated into the pleural space during inspiration when the intrapleural pressure is negative. Fluid, when present, follows the same motion and rises even higher on inspiration since the mediastinal shift narrows the intrapleural space. *2:* With the diaphragm intact it may be pushed down by the impact of positive intrapleural pressure at the moment of its expiratory relaxation. The inspiratory ascent is only apparent. On the other hand, with highly negative intrapleural pressure and only a small effusion the nonparalyzed diaphragm may actually be sucked into the intrapleural space on inspiration. The Kienboeck phenomenon is explained on the basis of the above mechanisms, and not by the diaphragm being inverted into the abdominal cavity by the weight of the pleural effusion. Inversion of the diaphragm was noted in only one of the 600 pneumothorax cases. This patient had phrenic-nerve paralysis in the presence of a positive intrapleural pressure.—*Paradoxical Pleural Pressures, Their Relation to the Kienboeck Phenomenon, B. P. Stivelman, Am. J. M. Sc., August, 1935, cxc, 256.—(E. M. J.)*

Vital Capacity in Health and Disease.—Following suggestions of previous writers that a comparison of vital-capacity readings in the same person in health and in later pathological conditions more accurately measures the value of the test than present methods of calculating variations from the normal by standards of measurement, the author studied a group of 482 healthy students, and compared the vital-capacity readings in two consecutive years. Deviations from the readings of the previous year proved to be decidedly smaller than those from the hypothetical vital capacity as calculated from the surface area formula of West. The reading of the previous year, therefore, constituted the more reliable basis for vital-capacity prediction. A group of 74 youthful patients with acute bronchitis was next studied. As might be expected the bed-cases exhibited a greater average loss than the ambulatory ones. From a statistical standpoint the loss in vital capacity in the ambulatory group could not be regarded as significant; in the bed-cases, however, the difference is almost three times the standard error of the mean, and probably is significant. Readings were also secured before, during, and after the onset of pneumonia in 3 cases, before and after one case of spontaneous pneumothorax, and before, during and after an attack of cardiac decompensation, the latter case showing a gradual diminution, with a gradual return to the original level as compensation became restored. In one case of mild pneumonia the fall was gradual, as opposed to the usual course in pneumonia. It is possible that cases of mild pneumonia masquerading as bronchitis may be more frequent than is generally recognized, and, if so, the vital capacity should assist in their recognition.—*Vital Capacity of the Lungs: Changes Occurring in Health and Disease, J. H. Arnett, J. Cl. Invest., September 5, 1935, xiv, 543.—(G. L. L.)*

Renal Function in Pulmonary Tuberculosis.—The results of renal-function tests in 90 patients with pulmonary tuberculosis were studied in the hope that such procedures would be of prognostic help in pulmonary tuberculosis. On each patient a 2-hour test, a water test, and a concentration test were carried out in the usual manner. In the interpretation of the results, the febrile cases were separated from the afebrile, and the former group further subdivided into those with far-advanced disease, but normal urinary findings, and those with advanced disease and abnormal urinary findings. The main group, comprising 80 patients, were those with no fever (except for an occasional daily evening rise of temperature to 99°, but not higher), with normal blood-pressures, no albuminuria, and a urinary sediment within normal limits. This group was subdivided into rather arbitrary age-groups, and limits proposed for what was to be considered the normal range of findings in each age-group for the 3 renal-function tests carried out. On this basis it was found that a characteristic impairment of renal function exists in tuberculous patients, namely, an impairment of tubular water-resorption. In the typical impairment, the specific gravity, in the 20 hour specimen, in the water test, and of the various specimens in the concentration tests, was low, even when evidence of delayed water excretion was taken into consideration. The difference found in response to these tests did not seem to be correlated with the extent of the pulmonary lesion, the duration of the disease, the degree of cavitation, if present, nor with activity, as measured by the sedimentation test. The estimation of the degree of renal-function impairment seems to be a measure of the degree of damage done by the toxaemia resulting from the pulmonary lesion. Tabulation of the results further showed that there did seem to be a positive correlation in cases of chronic pulmonary tuberculosis with little or no obvious activity between the subsequent course of the disease, whether toward recovery or fatal ending, and the response to the renal-function tests employed. In tuberculosis patients, with a temperature over 99.8°, a typical impairment was not observed, except, of course, in cases presenting frank evidence of chronic renal disease, such as albuminuria, casts or red cells.—*The Prognostic Value of Renal Function Tests in Pulmonary Tuberculosis, A. S. Kennedy, Canad. M. A. J., February, 1935, xxxii, 142.*—(*A. E. M.*)

Hydrogen Ion Values and Colony Morphology and Virulence of Tubercle Bacilli.—Twenty-five strains of human, bovine and avian tubercle bacilli were grown on Corper's glycerinated egg-yolk medium with congo-red, adjusted by means of phosphate buffers to pH 6.0, 6.4, 6.8 and 7.2. In all cases rough colonies appeared at pH 6.0–6.2. Smooth colonies predominated at 6.4 to 6.6 in the case of the human, at 6.4 to 6.8 in the case of the bovine and at 6.4 to 7.2 in the case of the avian strains. Intermediate colonies appeared in the human at 6.8–7.4 and in the bovine strains at 7.0–7.4. Growth in general was most vigorous at pH 6.0–6.2. When animals were inoculated with these colony variants, derived from a freshly isolated human strain, a highly virulent bovine strain, and a bovine strain of very low virulence, the rough colonies exhibited the least virulence, the smooth the greatest and the intermediate colonies an intermediate virulence. Smooth colonies from the bovine strain of low virulence are apparently not more virulent than the original undissociated culture. *Colony Morphology of Tubercle Bacilli. II. Influence of pH of Culture Medium on Colony Morphology and Virulence, K. C. Smithburn, Proc. Soc. Exper. Biol. & Med., 1935, xxxii, May, number 8, 1336.*—(*F. B. S.*)

Allergy and Immunity in Tuberculosis.—Immunity in the course of disease is defined as specific protection, either partial or absolute, developed by the host. The term "allergy" is used to express the inflammatory reaction which takes place when bacillary protein is brought into contact with the body-cells of a host previously sensitized either by natural infection or by artificial injection of living or dead bacilli. Allergy develops with immunity and remains as a "potential reaction" while infection exists in the body. It develops gradually after the primary infection, more promptly on reinoculation and remains as a factor throughout the course of the disease. For many years it was assumed that allergy was a part of the specific defense developed by the host against infection, but recently its attendant harmful effects have been so emphasized as to cause doubt as to its being in any respect a protective mechanism. *Properties of allergy: 1:* It develops coincident with specific defense. *2:* It does not permanently disappear as long as tuberculous infection is unhealed, but it may be temporarily lowered or abolished under a number of conditions, especially during certain intercurrent infections. Liebermeister and co-workers have shown that bacillaemia is common in tuberculosis and may occur at any time between first infection and death. It may play a rôle in sensitizing the cells to keep up the allergic state. *3:* It is not

stable and fixed but variable and inconstant. *4:* It is generally strongest during periods when bacilli are multiplying and tuberculous lesions most active, provided the patient's resistance is not overcome. It is particularly marked with the primary complex and early metastases, but, as a rule, advanced disease requires larger amounts of bacillary protein to cause a like response. *5:* Coincident with it, certain definite, specific protective phenomena occur: a more rapid tissue reaction; a migration of protective cells to the site of infection; increased phagocytosis; dilution of toxins by serous exudate; partial exclusion of oxygen by atelectasis and exudate; ability to ward off or abort new implantations; fixation of bacilli *in situ* or retardation of their passage through tissues. *6:* In disease followed by permanent immunity (*e.g.*, smallpox) a degree of cell sensitization remains permanently, evokes a feeble but accelerated reaction to revaccination, and is probably accompanied by protection against further infection. *Discussion of aspects of allergy:* The fact that its manifestations develop so early in tuberculosis, that it decreases as the extent of disease increases, that it magnifies the body's response to bacillary invasion or toxic products, that it fixes bacilli *in situ* or causes them to be extruded from open lesions, suggests a protective function. That it may result in tissue necrosis when severe is self-evident, but is it wholly undesirable and dangerous? Predominantly proliferative lesions are caused by bacilli few in number and low in virulence. Bacillary protein is produced in such small amounts that only a mild allergic inflammatory reaction occurs and only a slight and inadequate immunity develops. Repeated mild metastases are common. Clinical manifestations are mild until more extensive and severe metastases occur. There is a tendency to extension rather than self-limitation. Healing is slow and difficult but favorably influenced by tuberculin. On the other hand, in preponderantly exudative tuberculosis the infection is not co-extensive with the exudation, there are fewer structural changes and clearing by resolution is marked. Although bacillary substances are released in larger quantities, there is greater inflammatory reaction, symptoms are more acute, and healing may occur more rapidly and completely. The greater degree of allergy seems to be accompanied by greater specific defense. Should activity quiet down and the destructive process be checked, the two types tend to assume much the same status; necrosis in the one occurs in the midst of a primarily proliferative area, in the other, in area originally the seat of an exudative process. Considering these facts, is the allergic reaction fundamentally harmful or should it not be viewed as an integral and necessary part of specific defense, beneficial in mild degree? May not some of the harmful and destructive phenomena be, at least in part, due to other substances than those responsible for allergy? Circulating antibodies may, it is true, disappear soon after healing, but those fixed in the tissue cells may persist permanently. While instances are reported of negative tuberculin tests occurring following healing, we have no absolute data to show that this was not simply a marked desensitization. Also, while immunity has been produced without allergy and the latter has been removed without destroying immunity, these facts do not prove absence of relationship. Pottenger has observed an increase in the numbers of short as compared with long forms of bacilli in acute caseation and cavitation. He interprets these as young forms. He fails to find evidence that cell sensitization induced by tuberculous infection renders the host more susceptible to later infection. Nor is the evidence of complete healing of primary lesions conclusive. *Summary: 1:* The phenomena recognized as belonging to allergy are shown to have protective characteristics. *2:* Preponderantly proliferative tuberculosis is largely a cellular response in which allergy is mild and immunity inadequate. *3:* The therapeutic use of tuberculin in preponderantly proliferative tuberculosis causes mild allergy, checks the spread of the disease and hastens healing. *4:* Preponderantly exudative tuberculosis appears to develop a greater specific defense and heals more satisfactorily. *5:* As tuberculosis advances the patient becomes less sensitive to bacillary protein. *6:* The comparative ease with which endogenous reinfection can take place, as compared with the difficulties of exogenous infection of "immune" tissues, is discussed.—*The Relation of Allergy to Immunity, F. M. Pottenger, Tubercle, American Section, July, 1935, xvi, 458.*—(*A. P.*)

Koch's Phenomenon with Various Tubercle Bacilli.—In tuberculous animals intracutaneous injection of dissociated strains of tubercle bacilli (R and S forms) produced Koch's phenomenon. In animals with generalized tuberculosis R strains excited in the majority of cases an intense Koch's phenomenon, while S strains either failed to produce the phenomenon or produced it only in an atypical form. Nonpathogenic acid-fast bacilli and killed tubercle bacilli were unable to produce Koch's phenomenon

when used in the same dilutions as living and virulent tubercle bacilli. Rarely they excited hypersensitiveness in tuberculous animals when injected in excessive amounts. —*The Production of Koch's Phenomenon with Various Strains of Tubercle Bacilli, W. Pagel, J. Path. & Bact., July, 1935, xli, 89.*—(*E. R. L.*)

Tuberculosis in Allergic and Non-allergic Animals.—The technique of Bruno Lange, slightly modified, was used for studying the effect of the inhalation of virulent bovine tubercle bacilli on the course of tuberculous infection in the lungs of normal and previously infected guinea pigs. The apparatus used for inhalation is described. During the first days after the inhalation infection the allergic animals showed a very active cellular reaction around solitary tubercle bacilli, whereas the non-allergic animals even as late as 6 days after the infection showed the tubercle bacilli located in quite normal lung tissue without any surrounding cellular reaction. In both sets of animals the bacilli were found within the large mononuclear cells. In the allergic animals the individual bacilli appeared to be unchanged within the cells, whereas in the nonallergic animals the tubercle bacilli multiplied actively, so as to crowd the cells even on the 6th day after infection. At all stages of the infection there was a great difference in the number of tubercle bacilli in the two groups. Not until the 8th day after the infection did the cellular reaction appear in the animals that were not allergic to begin with. Because the tubercle bacilli were present in large numbers at this time, the reaction took place more rapidly, extending almost explosively and going on to central abscess formation, something that was seen exceedingly seldom and only to a slight extent in the allergic animals. These studies illustrate the importance of employing a technique which permits examination of infection arising from a single tubercle bacillus.—*Experimental Studies on the Development of Tuberculous Infection in Allergic and Non-allergic Animals. I. Development of Tuberculous Infection in the Lungs after Inhalation of Virulent Tubercle Bacilli, K. A. Jensen, G. Bindsley and J. Holm, Acta. Tuberc. Scandin., 1935, fasc. I, ix, 27.*—(*F. B. S.*)

Corneal Reactions to Tuberculoprotein and Tuberculophosphatide.—Tissue reactions to the components of the tubercle bacillus indicate that the protein fraction is responsible in a large measure for the acute exudative reaction, including much of the cellular response to the organism, and that the lipoids, particularly the phosphatide, stimulate the more chronic response and particularly the development of epithelioid cells and the lesions characteristic of tuberculosis. The present study deals with the action of small amounts of tuberculoprotein and tuberculophosphatide in normal and allergic guinea pigs. The cornea was chosen as the tissue in which to study the reactions to the above materials. The protein was purified TPT and the phosphatide A3-a, both prepared from human tubercle bacilli (H37). The phosphatide contained 0.229 per cent of nitrogen of undetermined nature. Tuberculous guinea pigs, which gave strong tuberculin reactions, received intracorneal injections of approximately 0.01 mgm. of tuberculoprotein in 0.005 cc. of physiological saline solution. A group of normal guinea pigs was similarly injected. Another group of tuberculous and one of normal guinea pigs received approximately 0.1 mgm. of the tuberculophosphatide emulsified in 0.005 cc. of physiological salt solution also in the cornea. One animal from each group was killed at 3, 7, 15 and 30 days after injection. The injected eyes were removed, sectioned and stained. A small additional group of normal and tuberculous guinea pigs received minute doses of tuberculoprotein combined with lecithin (egg) to see whether a phosphatide other than that from tubercle bacilli might not enhance the activity of the protein. It was found that the tuberculoprotein had a markedly toxic effect on the connective tissue of corneas of tuberculous animals and led to inflammation and partial degeneration (tuberculin reaction). Furthermore, it seemed responsible, probably indirectly, for the production of epithelioid cells in the later stages of the allergic reactions. Whether these cells were transformations of the mononuclear cells could not be positively determined; yet there were many intermediate forms which may well have represented successive stages of development from small mononuclears to the above types. Vascularization was apparently necessary to supply the needed mononuclear cells. Polymorphonuclears were able to migrate in large numbers from the limbus early in the reactions before vascularization had occurred; mononuclears were not. A positive indication of the vascular source of the mononuclears was their increased number in vessel lumina and the observation of some of them migrating through vessel walls. The fact that frequently they were most numerous about vessels was also in favor of their vascular entrance to the site of inflammation. In the amounts used the protein was practically inert in normal guinea pigs.

Tuberculophosphatide also caused an acute tuberculin-like reaction in tuberculous guinea pigs. Inasmuch as the preparation contained a small amount of nitrogen, believed to be an impurity and no part of the molecule, it was concluded that the reaction noted was probably a reaction to tuberculoprotein. The circumstance that the unknown substance was closely bound chemically seemed to explain the fact that the acute reaction to the tuberculoprotein alone was diffuse, while that to the tuberculophosphatide was localized. The phosphatide, as an emulsion, could not diffuse far from the site of injection, but the protein, as a solution diffused from the cornea into the limbus, iris and anterior chamber. In both tuberculous and normal animals epithelioid cells were present at the later periods and persisted longer than did those in most of the tuberculoprotein reactions. There was no constant qualitative or quantitative difference between reactions to the lecithin-protein mixture and to the equal amounts of tuberculoprotein alone in tuberculous animals. In tuberculous guinea pigs lecithin alone gave the same result as in normal animals. The findings confirm previous work indicating that in tuberculosis of the cornea most mononuclears taking part in the reactions at the site of injection come from the blood-stream, and that epithelioid cells arise from these mononuclears by a process of transition at the site of inflammation.—*Corneal Reactions of Normal and of Tuberculous Guinea Pigs to Tuberculoprotein and Tuberculo-phosphatide, S. W. Holley, Am. J. Path., November, 1935, xi, 937.*—(*J. S. W.*)

Effects of Tuberculous Reinfection.—Guinea pigs vaccinated with 5 mgm. *BCG*, or with 30 mgm. heat-killed bovine tubercle bacilli (Ravenel strain), as well as unvaccinated guinea pigs, were infected intratracheally with approximately 100 tubercle bacilli of the Ravenel bovine strain. Six weeks later all of the animals were killed and necropsied. Most of the *BCG*-vaccinated animals, which were allergic, showed a small number of fibrocaseous tubercles in the organs and lymph nodes, but failed to show any evidence of softening, and tubercle bacilli could not be demonstrated in the sections. The guinea pigs vaccinated with heat-killed tubercle bacilli, as well as the unvaccinated animals, showed extensive tuberculosis of the organs and lymph nodes, with well-marked softening, and in most cases numerous tubercle bacilli were demonstrable in the sections. Therefore, no relationship was demonstrated between the presence of allergy at the time of reinfection and the subsequent softening of the tuberculous process.—*Caseation and Softening in Tuberculosis of Vaccinated and Unvaccinated Guinea Pigs, J. D. Aronson, Proc. Soc. Exper. Biol. & Med., October, 1935, xxxiii, number 1, 82.*—(*F. B. S.*)

Allergizing Fraction of Tubercle Bacillus.—The tubercle bacillus has two properties, one which generates in virgin animal of first infection a heightened capacity toward inflammatory reaction to the reintroduction of tubercle bacilli, and another which elicits this tuberculin-like reaction in an animal already affected by tuberculosis. The first antigenic property of the tubercle bacillus is found in the insoluble residue which remains after repeated extraction of the finely pulverized bacilli by alcohol and ether, that is, after complete removal of all the lipoids, such as waxes, fats and phosphatides, followed by the removal of all the soluble proteins. This insoluble residue contains 9 per cent nitrogen, and on hydrolysis with dilute sulphuric acid yields 18 per cent of reducing substances. Normal animals treated with this substance not only show the heightened inflammatory reactivity on introduction of tubercle bacilli, but also give evidence of considerable protection against infection as shown by their greater longevity as compared to that of controls. However, this residue substance is incapable of eliciting a tuberculin reaction in animals already sensitized to the bacillus. The soluble proteins on the other hand elicit the tuberculin reaction in the allergic animal but cannot generate this altered reactivity in the virgin animal.—*Untersuchungen uber den Träger der umstimmenden Substanz des Tuberkelbazillus, F. Lindner and L. Oelrichs, Ztschr. Immunitätsforsch, November, 1935, lxxxvi, 181.*—(*M. B. L.*)

Heat-Stability of Tuberculin.—It has long been realized that tuberculin is extremely heat-stable. Autoclaving and prolonged heating at high temperatures reduce its activity surprisingly little,—about 50 per cent. Also tuberculoprotein, prepared by Seibert's method, had a similar high degree of heat-stability. Hence it appeared advisable to find out to what extent minute amounts of tuberculin might remain adherent to cleaned glassware and other apparatus. It is already known that other biological products, such as concentrated diphtheria antitoxin, adhere with considerable tenacity even after several washings, so that the precaution is advised of boiling such utensils as syringes for ten minutes after washing and before using for other purposes. *Description of experiments:* Apparatus was deliberately

contaminated with undiluted Old Tuberculin of International Standard of potency, then washed out thoroughly and in many cases also autoclaved. Test samples of washings were injected intracutaneously into tuberculous guinea pigs, whose sensitivity was found to vary up to between 1 in 8,000 and 1 in 25,000. A 250-cc. bottle, pipettes, a Berkefeld-N filter-candle, were employed. After washing with tap-water and autoclaving, usually half an hour at 15 lbs., borated buffer solution was used to obtain material to inject the guinea pigs. Repeated autoclaving, in the case of the Berkefeld filter, appeared to multiply the strength of the tuberculin present after washing. This is probably due to "elution" of the tuberculin absorbed on to the candles. It collects in the moisture of their pores during the resting period. In another series of experiments, syringes used for dilutions of 1–50,000 to 1–100,000 tuberculin were washed ten times under the tap and steamed. Saline solution to the amount of 0.2 cc. was taken up and injected into a Mantoux-positive volunteer, who, surprisingly, gave faint but definite reactions. Repetition of this in the different types of pipettes and dilutions often yielded positive results. These data suggested that special syringes should be reserved for use not only with tuberculin but with particular dilutions; these could be conveniently ringed in bands of different colors for different dilutions. Parish and O'Brien have been unable to find a simple but reliable method of removing tuberculin or tuberculoprotein from either syringes or filter candles. As similar results hold with Seibert's tuberculoprotein, the "tenacity" is not due to glycerin. *Summary:* Tuberculin adheres to apparatus with exceptional tenacity and is extraordinarily heat-stable. Every trace is not removed by either thorough washing or autoclaving. All glassware and filter candles used for tuberculin should be clearly marked and restricted to that purpose. Also, separate syringes should be reserved for different dilutions. Tuberculin, in all stages of preparation and preservation, should be kept rigorously apart from other products.—*The Heat-Stability and "Tenacity" of Tuberculin, H. J. Parish and R. A. O'Brien, British M. J., May 18, 1935, no. 3880, 1018.*—(*A. P.*)

Note: It may be mentioned that, between 1910 and 1914, during many series of experiments on tuberculoallergy and cross-sensitization, a simple and infallible technique was used to prevent the clinging of protein particles to instruments and appliances. Boiling, which coagulates, should never be done until all organic material is removed from all and every piece of apparatus used. All glassware, after prolonged and thorough washing in *cold* running water, was placed for days and perhaps weeks in picric-acid-potassium-bichromate fluid,—a true corrosive for all organic particles. This would include culture-tubes and flasks, pipettes, syringes (Luer), etc. Berkefeld candles were washed and washed and washed by repeated filtering of water; again, any single candle was always used for a single type (strain) of organism and no other. Needles were always fresh and new for each injection, etc. All this preliminary to sterilization.—*A. K. K.*

Serological Specificity of Caseous Matter.—On the intravenous administration to rabbits of cooked watery extracts of human or bovine caseous material antibodies appear in their serum which react in the complement-fixation test with extracts of caseous material of these two species but little if at all with extracts of their normal organs or blood. The antisera against caseous material therefore are not species-specific but specific for caseous matter as such. On the immunization with alcoholic extract of caseous matter, to which pig-serum is added, the ensuing antibodies are rarely specific for caseous matter. The immune sera produced by treatment with caseous matter, while rarely reacting with extracts of normal organs, often react with those of cancerous and purulent material. The caseous-material antibodies can be absorbed by the homologous antigen. Normal lung tissue and blood reduce these antibodies only insignificantly. Alcoholic extracts of positive tuberculous sputum react in the complement-fixation test with antisera of rabbits treated with caseous matter. Negative sputa rarely react. In the sera of rabbits immunized with watery extracts of liver, carcinoma antibodies appear, which react in the complement-fixation test with alcoholic extracts of certain carcinomata and bovine and human caseous material, but not with the extracts of the normal organs employed.—*Untersuchungen über die serologische Spezifität pathologisch-veranderter Organgewebe, L. Hirszfeld and W. Halber, Ztschr. Immunitätsforsch., August, 1935, lxxxv, 447.*—(*M. B. L.*)

Survival of Tubercle Bacilli *in Vacuo*.—The following study was suggested by the idea that prolonged high-vacuum treatment would kill tubercle bacilli and thus afford a noninfectious vaccine of greater antigenic value than that possessed by vaccines obtained by methods more commonly employed. In the experimental work avian

tubercle bacilli were used exclusively and grown on glycerin-agar. The bacilli for the vacuum test were transferred, without drying or washing, to a Pyrex glass tube, and the organisms shielded from the light by painting the surrounding part of the tube with black enamel. The open end of the tube was then carefully drawn to a fine capillary neck in a torch flame. The full length of the tube was then enclosed in a sleeve of black paper. The neck of the tube was now glass-sealed to the vacuum line of a high-grade mercury pump, and the latter was allowed to operate for from twelve to sixty hours, depending on the particular experiment. The rarefaction of oxygen obtained consistently reached or exceeded one-billionth of an atmosphere. With such vacuum established the tube was sealed by a needle flame and was removed for the period of storage. A high vacuum remained throughout each experiment, as shown by the occasional use of the high-frequency-spark test and by the collapse of a soft rubber sleeve in which the tube was ultimately opened. In some of the experiments, to obtain the maximal removal of ultimate traces of all gases a chemical "getter" was also used. For this purpose metallic magnesium was employed on account of its powerful affinity for oxygen. The tests of the viability of the tubercle bacilli recovered from the vacuum tubes were made both by culture on glycerin-agar and inoculation into pigeons. Following injection the pigeons were kept for from four to six months and then killed, autopsied and their tissues investigated. The method of Cooper was used for staining microscopic sections for tubercle bacilli. *Results:* In the first experiment bacilli subjected to a high-grade vacuum at room temperature for up to eight months still produced generalized tuberculosis in pigeons. In the second experiment the bacilli, similarly deprived of oxygen but kept at incubator temperature for eighty days produced massive tuberculosis in pigeons (and rabbits). In the third experiment the bacilli, after being subjected to severest oxygen deprival (use of a "getter") for from seven to forty-eight days, not only yielded positive cultures but produced tuberculosis on inoculation. In the last experiment, in which oxygen deprival for several months was accompanied by maximal desiccation with phosphorus-pentoxide powder, the bacilli, when transferred to culture medium, grew luxuriantly and also caused tuberculosis when injected into pigeons. Emphasis must be placed on the fact that in performing these experiments special attention was given to two factors: (1) the subjection of the tubercle bacilli to a really drastic oxygen deprival and this in the absence of a complicating fluid of suspension or gross mass of culture medium, and (2) an actual comprehensive test of the viability of the bacilli after such oxygen deprival. The results indicate that avian tubercle bacilli retain viability under conditions such that the amount of molecular oxygen present is immeasurably small.—*The Survival of Tubercle Bacilli Subjected to a Vacuum of High Order, T. S. Potter, J. Infect. Dis., September-October, 1935, lvii, 149.*—(*J. S. W.*)

Lysis of Tubercle Bacilli *in Vitro*.—Extreme variants *Ra* and *Rv* from a dissociated H37 culture were studied. To indicate virulence or avirulence the letters (*v*) and (*a*) were appended to the *R*. These variants were grown upon gentian-violet-egg and plain glycerol-egg media of the following pH: 5.0, 5.5, 6.0, 6.2, 6.5, 6.8, 7.0, 7.3 and 7.5. No colonies grew on flasks where the pH was below 5.5. Cultures of the *Rv* variant during the first three months showed typical wrinkled or stippled colonies that were slightly raised, with spreading veil-like peripheries. Still later these colonies on media of pH 6.0, 6.2 and 6.5 became slightly moist, and their central portions liquefied until some of the colonies completely disappeared. There was no evidence of lysis in the *Ra* variant.—*Lysis of Tubercle Bacilli in Vitro, W. Steenken, Proc. Soc. Exper. Biol. & Med., November, 1935, xxxiii, 253.*—(*F. B. S.*)

Dissociation of B. Friedlander and B. Tuberculosis.—It is not an uncommon observation that the virulence of *B. Friedlander* and *Mycobacterium tuberculosis* is greatly influenced by the pH of the culture medium. The object of the present study was to determine what pH was most favorable for dissociation and stabilization of different variants once dissociated. The results show that *B. Friedlander* dissociates best in media of acid pH., that *M. tuberculosis humanus* (H37), on acid synthetic media buffered with N/10 double potassium-phosphate salts, and on weakly buffered glycerol-beef-broth, becomes attenuated, and on a buffered alkaline synthetic medium, using double potassium-phosphate salts, retains its pathogenicity; that acid-glycerol-potato-bile medium favors the attenuation of *BCG*, and that, if grown on a buffered synthetic medium over a period of a year or more, it may regain its virulence; and that stock medium, weakly buffered above pH 7.0 standing in an incubator, tends to become acid.—*The Influence of the pH on Dissociation of B. Friedlander and M. Tuberculosis, W. Steenken, Jr., J. Infect. Dis., May-June, 1935, lvi, 273.*—(*F. G. P.*)

Media for Bovine Tubercle Bacilli.—The Löwenstein medium, containing asparagine, potato flour, egg, malachite-green, 0.75 per cent glycerine, etc., was found to be most satisfactory for the cultivation of bovine tubercle bacilli. Hohn's medium was less satisfactory, and the Petroff medium was unsatisfactory for isolating bovine strains, but quite suitable for cultivating human bacilli. Glycerine in increasing concentrations was found to be distinctly inhibitory for the bovine tubercle bacillus. It increased the size of colonies of the human type, but reduced their number. The growth-promoting power of the different carbohydrates related to glycerine was studied. Galactose was the only one found to stimulate the growth of the bovine bacillus. The Löwenstein egg medium, without glycerine, but with the addition of 4 per cent galactose and 0.15 per cent alanine, was found to be of advantage in the isolation of 126 fresh bovine strains from various types of tuberculous material.—*An Egg Medium Containing Galactose for Cultivation of the Bovine Type of Tubercle Bacilli. Comparative Investigations between Petroff, Hohn and Löwenstein Media, J. Frimodt-Möller, Acta. Tuberc. Scandin., 1935, fasc. I, ix, 47.*—(*F. B. S.*)

Dispersion of Tubercle Bacilli in Infection.—Aqueous extracts of testicle contain a substance which produces a rapid and pronounced increase in the permeability of the dermis and connective tissues for injected fluids and suspensions. Toxins, suspensions of bacteria, and viruses may, with the aid of such a spreading agent, be dispersed through a greatly increased area of skin, and this dispersion brings about definite alterations in the nature of the resulting lesions. The dispersion of large amounts of living bacteria augments both the size and severity of the lesion which developes, as compared with that produced by like numbers of bacteria injected in saline solution. The present paper deals with the effects of such dispersion on tuberculous infection in guinea pigs and rabbits. Dermal infections were found most suitable as the extent of dispersion could be readily measured. Human, bovine and avian tubercle bacilli were the infecting agents used. Also *BCG* and defatted bovine tubercle bacilli were employed. The spreading agent was a filtered extract of bull's testicle. Mixtures generally contained equal parts of bacillary suspension and testicular extract. The skin lesions in rabbits and guinea pigs following intracutaneous injection of tubercle bacilli (5 strains) were greatly increased in size and severity when testicular extract was added to the inoculum. Such enhancement was followed by a more widespread and rapidly progressing disease only when virulent strains were employed. It has been shown with many bacterial strains that when the number of bacteria injected falls below a certain critical concentration, the action of testicular extract results in the suppression of the lesion rather than an enhancement of it. Attempts, however, to suppress the development of skin lesions by the injection of either normal or tuberculous rabbits with very small quantities of tubercle bacilli mixed with testicular extract were unsuccessful. These findings emphasize the fact that, owing to their peculiar chemical constitution, the tubercle bacilli are uniformly capable of producing the characteristic lesions when introduced into the tissues, irrespective of their ability to invade the tissue of the particular host chosen. The skin reactions of tuberculous guinea pigs to tuberculoprotein MA-100 were greatly increased in size and markedly reduced in intensity by the addition of testicular extract to the protein solution. Any toxic effect of the tuberculoprotein is unaltered. The dispersion of tubercle bacilli through the skin of tuberculous rabbits resulted in a marked enhancement of the Koch phenomenon, but was not followed by any extension of the new infection to the viscera. Tuberculous rabbits injected on two occasions with dead tubercle bacilli suspended in testicular extract showed an increased resistance to the disease when compared with controls receiving dead bacilli suspended in saline solution. In animals previously infected with a small dose of virulent tubercle bacilli, reinfection with these bacilli usually results in a delay in the further development of visceral lesions. The resistance conferred on tuberculous guinea pigs by such superinfection was greatly increased when the bacilli employed were dispersed through the skin with testicular extract. The injection of large quantities of testicular extract parenterally in recently infected guinea pigs had no effect on the rate of progression on the distribution of the lesion. The partial immunity conferred upon guinea pigs and rabbits by vaccination with heat-killed tubercle bacilli was increased as a result of dispersion of the vaccine through the skin with testicular extract. The action of the extract as a dispersing agent in experimental tuberculosis may be likened to that of an amplifying device. The factors of host immunity and bacterial virulence determine the nature and direction of the response to infection, but the degree of dispersion of the bacilli in the tissues determines to a large extent the magnitude of the response.—*The Degree of*

Dispersion of the Bacillus as a Factor in Infection and Resistance in Experimental Tuberculosis, R. M. Thomas and F. Duran-Reynals, J. Exper. Med., July 1, 1935, lxii, 39.—(J. S. W.)

Virulence and Colony Form in Tuberculosis.—Does the virulence of various bovine and human strains of tubercle bacilli bear any relationship to the morphology of colonies isolated from animals inoculated with them? Eight human and 11 bovine strains were used in the virulence tests. In order to classify the strains it was necessary to inoculate both rabbits and guinea pigs with each culture. Each animal received 0.1 mgm. of organisms; rabbits were inoculated intravenously, guinea pigs subcutaneously in the right groin. Two rabbits and 2 guinea pigs were inoculated with each bacterial suspension. Half of each set were killed at 30 days and all survivors at 60 days. At autopsy the extent and microscopic appearance of the lesions produced by the various strains in the lungs, bone-marrow, lymph nodes and visceral organs were noted, and the sum of these data gave a figure for each animal which represented quite accurately the extent of the tuberculosis present or the virulence of the organism in question. All the strains of human tubercle bacilli described in this report as recently isolated from clinical cases proved to be virulent and showed but slight differences in pathogenic properties. Neither did they show extreme variation in virulence when compared with strain H37 isolated many years ago. Among 11 bovine strains cultivated *in vitro* for varying periods, there was a much wider range in virulence, some being so attenuated as to give regressive lesions in both rabbits and guinea pigs, while other strains were highly pathogenic. In general, the more recently isolated strains were the more virulent. Attenuation occurs with prolonged *in vitro* cultivation, but the rate of attenuation is apparently not the same for all strains. These observations make it clear that in order to classify a given mammalian strain, the virulence of which has not been recently tested, it is necessary to inoculate both rabbits and guinea pigs. A human strain of full virulence produces progressive tuberculosis in guinea pigs, but not in rabbits. A bovine strain of full virulence produces progressive tuberculosis in both rabbits and guinea pigs, whereas bovine strains of low virulence produce retrogressive lesions in these animals. Therefore, if a strain of mammalian tubercle bacilli be inoculated into rabbits, and if it produces lesions which regress, it does not follow that it is a human type bacillus unless it be shown also that the organism produces progressive tuberculosis in guinea pigs. Examinations were also made to determine the relative numbers of acid-fast bacilli in the lungs, spleen, and bone-marrow of each animal. A very definite relation was found between the number of organisms in the lesions and the virulence of the strain. The strains of greater virulence showed the greater numbers of bacilli and the strains of least virulence showed the fewest (or none). Most of the stained organisms were later proved to be viable, and a large number of them therefore indicates that multiplication has taken place. In view of the fact that differences in virulence may depend on the colony form, the question was asked, do strains of tubercle bacilli of low virulence produce smooth colonies, and, if so, are the smooth colonies produced in as great number as in the case of highly virulent organisms? Cultures were obtained from the necessary animals on egg and egg-yolk media using treated and untreated material. Untreated material was seeded, as the use of H_2SO_4 or NaOH inhibits the development of smooth colonies. Studies of these recovered cultures demonstrated that, in the case of bovine bacilli, virulence is correlated with three phenomena: namely, the number of bacilli which can be stained in tissues of inoculated animals, the number of organisms recoverable in cultures from the tissues, and the proportion of smooth colonies in these cultures. Some smooth colonies, however, were present in strains having little or no pathogenicity. One example is cited of an avian strain which had lost its virulence while retaining the smooth colony form, indicating that, although pathogenicity is usually correlated with smooth colony form, it is not necessarily so. Smooth variants, devoid of virulence, do occur. In the cultures recovered from animals inoculated with human strains there was no correlation between the number of organisms seen in the stained sections and the number of positive cultures or number of colonies recovered from the tissues. Smooth, rough and intermediate colonies occurred in cultures of each human strain. The smooth colonies were most numerous in cultures from guinea pigs. In the cultures from rabbits, colonies with granular (rough) characteristics predominated. In the comparison of the effect of the human strain on rabbits and guinea pigs, it was shown that native resistance (of the rabbit) was associated with a power to dissociate the inoculated bacilli into a greater proportion of rough forms, and then to destroy them. Culture from the tissues of rabbits 60 days after inoculation were consistently negative.—*The Colony Morphology of Tubercle Bacilli. III. The Rela-*

tion between Virulence and Colony Form, K. C. Smithburn, J. Exper. Med., November 1, 1935, lxii, 645.—(J. S. W.)

Dissociation of *M. Phlei*.—In the light of present knowledge it seems that saprophytic acid-fast bacilli are not pathogenic for man. The introduction of large numbers of organisms into the peritoneal cavity of guinea pigs leads to the formation of localized nodules, which eventually soften, containing purulent, somewhat caseous, masses. Typical tubercles with giant-cell formation are observed only under special injection methods (Lubarsch). Moderate doses do not cause death, but very large doses frequently lead to a fatal termination. Environmental conditions play an important part in the variability of saprophytic acid-fast bacilli. The present study deals with the variability of *Mycobacterium phlei* (timothy-grass bacillus). The variability of this organism was studied on gentian-violet-egg medium directly and after several passages on Proskauer and Beck's medium of pH 7.6. More than half a dozen different colonies were observed under such cultivation. These variants have been carefully studied, but up to the present no conclusion is possible as to their significance. Rapid passage of the organism on synthetic medium containing heat-killed "R" variant showed a definite change in the growth appearance. The floating pellicles became gradually lighter in color, losing their chromogenicity, thus becoming creamy white. Cultivation in synthetic media containing 20, 10 and 5 per cent normal sheep-serum produced in the 5 per cent serum bottles a veil-like growth much lighter in color than the growth of the serum-free medium. Morphologically, the control growth was composed of short thick bacilli, while that from the serum medium was slender and long with occasional filamentous rods. It is possible that most of the saprophytic acid-fast cultures mentioned above are not different species, but variants from what appears to be one single strain. It seems that at present we should abandon any attempt to devise a classification of the group until we acquaint ourselves with the utmost limits of variability which exists freely among saprophytic acid-fast organisms. No attempt was made to label the variants obtained, as they are too numerous and many of them unstable. Dissociation of *M. phlei* is not a simple phenomenon of splitting "S" from "R" types, etc. There are many transitional stages which could have escaped detection. These transitional colonies are so unstable that topographical appearances may be modified within a few days. The chromogenicity of the variants is also an unstable characteristic. The medium, light, temperature, and carbon-dioxide and oxygen supplies in the cultures play important parts in the development of this characteristic. The most uniform results were obtained when the special flat culture flask was used for the solid medium. It is also important to use uniform medium constituents and the proper handling of cultures. Not a single yellow or white variant, when inoculated into guinea pigs, produced progressive disease. However, some progressive disease in guinea pigs inoculated with modified *M. phlei* was produced by using a special method of inoculation, but the results were inconstant and variable. This failure, however, does not eliminate the possibility of the enhancement of virulence. If such enhancement of virulence does take place in nature it should be possible to repeat it in the laboratory.—*Biological Studies of Saprophytic Acid-Fast Organisms. I. Dissociation of Mycobacterium Phlei, S. A. Petroff and W. Steenken, Jr., J. Infect. Dis., May-June, 1935, lvi, 277.—(F. G. P.)*

Smegma Bacillus and Tuberculosis.—Three groups of 8 rabbits each were treated as follows: Group A received 4 intratracheal inoculations of 10 mgm. of young viable smegma bacilli at 2-day intervals, and twelve days following the last inoculation, 2.5 mgm. of virulent bovine tubercle bacilli. Group B received comparable treatment with smegma bacilli only, and group C received only the final inoculation of bovine tubercle bacilli. All rabbits in group B survived the experiment and no lesions could be demonstrated in them. The average life-span of the tuberculous animals (group C) was 66 days, as compared with 175 days plus for the smegma-vaccinated tuberculous rabbits (group A). The animals in which treatment with smegma bacilli preceded the inoculation with tubercle bacilli showed less caseation and more fibrosis in the lungs than did the rabbits receiving tubercle bacilli alone. The authors believe that artificial immunity to tuberculosis is best induced, not by the tubercle bacillus itself, or by any of its fractions, but by a living nonpathogenic acid-fast organism, such as the smegma bacillus.—*Immunological Properties of the Smegma Bacillus in Experimental Tuberculosis in Rabbits, E. DeSavitsch, K. L. Burt and Molly H. Radford, Proc. Soc. Exper. Biol. & Med., October, 1935, xxxiii, 180.—(F. B. S.)*

Note: Here may be recalled the not dissimiliar work, done by Baldwin and Krause as far back as 1910 to 1913 (and later). (*Cf.* a short synoptic report in *Tr. Nat. Assoc. Study & Prev. Tuberc.*, 1913 (Krause).) In cross-hypersensitization work, Krause al-

ways found the Saranac Laboratory strain of *B. smegmatis* to give more vigorous allergic reactions with *B. tuberculosis* than in the case of any other so-called nonpathogenic acid-fasts. Here and in other places the implications, as regards tuberculoimmunity were wont to be discussed. Hypothetically, and on the basis of a vast amount of experimental work of a quarter-century ago, the commentator would welcome the above experiments as largely confirmatory. But, there is a long bridge—still unspanned—between a "lead" and demonstration. *Cf.* also the several essays on the nonpathogenic acid-fasts, transmutation, relationships, immunity factors, in the long series of *Essays on Tuberculosis* that appeared in the *Journal of the Outdoor Life* from 1917 to 1924.—*A. K. K.*

Pyrexia in Pulmonary Tuberculosis.—It was formerly held that active pulmonary tuberculosis always gave rise to some abnormality of temperature, and various elaborate methods of temperature-taking were evolved to detect slight variations. With the advent of the X-ray, especially the serial X-ray, our conceptions of the relation of the temperature to spread of disease have altered fundamentally, and this is now regarded as the most accurate single method of determining progression or retrogression of the disease. Temperature readings are still significant and valuable. Wingfield's classification has been used at the Brompton Hospital Sanatorium, Frimley (England), since 1932. It is, briefly, as follows: *1: Secondary lesion:* A local allergic tissue reaction due to deposition of bacilli, probably haematogenous. It may disappear or progress to *2: Intermediate lesion* which corresponds roughly to active fibrocaseous disease. *3: Tertiary lesion* is a healed or nonprogressive intermediate lesion, which, however, may become secondarily infected by other organisms. *1: Secondary lesions:* The temperature disturbance is apt to vary with the size of the foci, which in turn depends on (1) number of new bacilli deposited, and (2) allergic state of the pulmonary tissue. The lesions are divided into small, medium and large, and the first may be unattended by rise in temperature or clinical symptoms. Usually the large have a rather acute onset like lobar pneumonia, but subside by lysis, generally within fourteen days. *2: Intermediate lesions:* The temperature-chart for at least several weeks may give no indication of the spread, as shown by serial X-ray films, and the patient may appear to be in good health. When bronchial ulceration occurs, then fever and other symptoms associated with chronic pulmonary tuberculosis appear. The fever is intermittent and shows a diurnal swing. It tends to settle gradually with bed-rest. While pyrexia continues new secondary lesions may appear with a sudden increase in height and swing. *3: Tertiary lesions:* Patients with these are usually afebrile, unless there has been a long period of illness and much lung destruction. Many of these run a mild pyrexia, although serial X-rays appear stationary. In some, there are characteristic exacerbations, with increased cough and sputum. Certain patients with "late cavitation" show sudden steep rises and swings followed by a large amount of purulent sputum. Capacity for exertion is diminished. Myers attributes these attacks to secondary pyogenic infection. *Conclusions: 1:* The various types of lesion in chronic pulmonary tuberculosis give rise to characteristic temperature changes. *2:* Spread of disease may occur in the absence of pyrexia. *3:* Many cases of quiescent pulmonary tuberculosis suffer from frequent bouts of pyrexia or constant mild pyrexia without any evidence of spread. *4:* It is possible that pyrexia is often caused by secondary infection of the tuberculous lesions. *5:* Serial X-ray films are the most reliable guide to the spread or retrogression of the actual tuberculous lesions, but the temperature chart gives essential and valuable information.—*Significance of Pyrexia in Chronic Pulmonary Tuberculosis, M. Myers, British M. J., August 10, 1935, no. 3892, 250.*—(*A. P.*)

Diaphragmatic Paralysis and Cough.—The study is not concerned with expectoration but only with what happens to the force of the cough. For this purpose both sides of the diaphragm were paralyzed. Bilateral thoracotomy was performed on a healthy young adult dog (a total of 4 were used) and silver wires were looped around each phrenic nerve and the chest was closed. Four days later under nembutal anesthesia a T-shaped cannula was placed in the trachea. To one end was attached a Krogh inspiratory valve and to the other an expiratory water-valve. Connected to the latter was a tube of smaller diameter leading to a Brodie bellows, with a lever recording on a smoked drum. A vent was provided to permit collapse of the bellows, and easy exit of the expired air, a small fixed portion of which was delivered to the bellows. Cough was produced by stimulation of the larynx with Dakin's solution or by mechanical means. Three responses were recorded before evulsion of the phrenic nerves by extraction of the silver wires from the chest. The experiment suggests that there is no essential difference in the force of maximum expiratory blast before and after phrenicectomy. It is generally assumed that, following lapa-

rotomy, cough is restricted by the limited capacity of the abdominal muscles to exert pressure on the peritoneal cavity. A healthy adult dog was anaesthetized and connected to the apparatus. No difference in response to stimuli was noted when the lower part or the entire abdomen, exclusive of the costal margins, was tightly strapped. Only after restricting the excursion of the ribs did cough become less forceful. There is evidence that when the entire diaphragm is nearly in the full expiratory position, it affords neither help nor hindrance to the force of the expiratory blast.—*The Effect of Diaphragmatic Paralysis upon the Efficiency of Cough, J. Fine and A. Starr, J. Thorac. Surg., June, 1935, iv, 525.*—(*L. F. B.*)

Oxygen Treatment of Haemoptysis.—Oxygen was injected subcutaneously in quantities of from 300 to 600 cc. in 7 patients with haemoptysis, five of whom had tuberculosis. In four of them, the treatment was effective in controlling the haemorrhage; in three it was not. A feeling of euphoria was very evident following the injections. The coagulation time decreased markedly in all cases after the injection of oxygen. Blood analyses made before and after the injections revealed no influence on either the corpuscle count, the haemoglobin or the platelet count. The apparatus used was that built by Bayeux in 1911.—*La Oxigenoterapia de las Hemoptisis, J. J. Spangenberg, L. Munisti and A. Ardaiz, Rev. Asoc. Med. Argentina, February, 1935, ii, 36.*—(*J. R. P.*)

Signs of Pulmonary Cavities.—Most of the pulmonary cavities, irrespective of whether they are tuberculous, bronchiectatic, acute suppurative, or neoplastic in origin, do not reveal their presence by pectoriloquy and amphoric breathing. The 350 cases of pulmonary cavities studied fall into four groups according to auscultatory signs: (1) cavities with classical signs, 29.7 per cent; (2) mute cavities over which no suspicious signs of any pulmonary lesion can be elicited, 9.4 per cent; (3) relatively silent cavities which are lacking in the classic signs, but over which other adventitious sounds are heard, such as altered breath-sounds, modified whispered voice, inspiratory râles over a limited area, 50.6 per cent; and (4) intermediate cavities whose signs alternate between those of groups 2 and 3, 10.3 per cent. In about 80 per cent of all pulmonary cavities the stethoscope was sufficient to diagnose or at least to suggest the presence of a cavity. In many instances the stethoscope was more informative than the roentgen-ray alone, since cavernous breathing always indicates a cavity even if it cannot be outlined in the ordinary roentgenogram. The factors of primary importance in the production of the variable signs of cavities are the communicating bronchi, consistence of the capsule of the cavity, the topographic relations, the surrounding lung tissue, and the medium of conduction. The absolutely mute cavities can be diagnosed only by roentgen-ray. They usually have a fair prognosis. The most significant and common signs of early cavitation with its soft yielding nonvibrating walls are modified breath-sounds and localized coarse râles heard on ordinary inspiration. Such lesions are easily amenable to collapse therapy. Cavernous breathing generally indicates an older cavity, be it tuberculous or nontuberculous, with fibrosed, rigid walls which render it refractory to medical treatment; only radical surgery is able to close completely such a cavity. Serial roentgenograms and physical examinations are essential for the determination of the proper therapeutic procedure to be employed.—*Variable Auscultatory Signs of Pulmonary Cavities, R. A. Bendove, Am. J. M. Sc., July, 1935, cxc, 60.*—(*E. M. J.*)

X-Ray Diagnosis in Pulmonary Disease.—The advances in this field in a quarter of a century have been remarkable. With the earlier coil-sets it was not possible to take films of the lungs at rest, and fluoroscopy was more valuable, while latterly the film is almost exclusively relied upon. This paper deals with technique, the appearance and differentiation of puzzling cases, and with silicosis in particular. It is emphasized that no chest examination is complete without proper roentgenographic examination and that a proper interpretation of the abnormal demands familiarity with the normal lungs in people of all ages and occupations. *Technique:* Fluoroscopy should not be too frequently practised. Its chief value is in demonstrating diaphragmatic movement, localizing abscess or hydatid, and controlling lipiodol instillation. To be properly carried out, the operator should be in complete darkness for ten minutes by the clock beforehand. A rough test is to look at the wrist-watch, as, when the figures appear dazzlingly bright, the eyes are accommodated. In routine chest roentgenography, stereoscopic posteroanterior films are most valuable and laterals only occasionally. Films should be taken at a distance of 6 or 7 ft., with a 4½-inch vertical tube shift, the centre for the lower film being interscapular and direction slightly downward. The upright position should be used with hands in front and shoulders drooped forward. Exposure should be at the end of ordinary, not deep, inspiration. With the exception of the rotallix tube, there is none which can economically

stand more than 300 milliamperes at 70 kilovolts: using this set-up at a 7-foot distance, excellent films of the average workingman are obtainable, at 1/30 second. A 20-kw. metallix tube can be used and is usually satisfactory, despite the coarse focus. Violent contrast in chest films is not desirable and the spinal structure details should not be too clearly visible. *Morphological diagnosis: 1: Apical scars* are seen as dense shadows and are common in workingmen. They probably evidence healed tuberculosis, never appear to break down and fresh lesions usually develop elsewhere. *2: Effusions* should not be difficult to diagnose, unless atypical, such as the interlobar and localized triangular. Lateral films may here be of value. Mesially located effusions (near the mediastinum) are rare. *Hydatid lesions'* shadows are usually spherical and cause more depression of the diaphragm when in this region. They may be rounded on the visceral and flattened on the parietal side. *3: Bronchiectasis* can usually be demonstrated in the ordinary film unless behind the heart or in the costophrenic angle. Lipiodol instillation, when needed, should be by the supraglottic rather than the cricothyroid route. The amount should not be too large. *4: Fungus infections* consist chiefly of (1) yeast infections and (2) actinomycosis. In the former, there is bilateral uniform fuzziness with scattered areas of bronchopneumonic consolidation. Actinomycosis is first localized to one lobe, later extending in all directions and frequently involving the chest-wall, with typical boggy oedema. *5: Tuberculosis* practically always, in adults, starts in the upper lobes and early lesions show fluffy mottling peripherally, fine striations being due to fibrous tissue. It is not always possible to distinguish between active and quiescent lesions, but an experienced observer may form a fairly accurate estimate. Miliary tuberculosis may be uniformly distributed, even without physical signs. *6: Silicosis* occurs in rock choppers, coal-miners, cement-workers, asbestos-workers and tool grinders. Inhaled dust is dangerous in proportion to its silica content, producing a nodular fibrosis. One silicate of potassium and aluminum (sericite) appears to produce inflammation and necrosis (Gardner) but no fibrosis. Asbestos, a magnesium silicate, produces diffuse, not nodular, fibrosis. Hawkesbury sandstone contains over 80 per cent free silica, metalliferous ores 20 to 60 per cent, coal 2 to 4 per cent. However, coal-miners may cut through seams of rock with over 30 per cent silica, and in many mines sandstone dusting is used to carry down the fine coal and minimize the risk of explosions. With a high silica content of dust, the onset of the disease is apt to be more rapid, also, in lungs with damaged lymph-circulation: the extent of the X-ray lesions is no measure of the physical disability. Only the finer particles (under 5 micra diameter) reach the alveoli. These go into colloidal solution and set up a chemical tissue irritation, possibly destroying the phagocytes which take up inert dusts, such as coal. The silica nodule is like the tuberculous one but never caseates. The nodular fibrosis is bilateral and spreads symmetrically along the bronchial tree, the apices being involved only late. The early changes are indistinguishable from those in catarrhal conditions, asthma and the aged. When well developed, there is characteristic "stippling" but a "presilicotic condition" cannot be diagnosed. Once established, the condition advances and pleurisy is a common complication, with extensive adhesions. Most silicotics develop tuberculosis, usually fatal. The appearance of dense mottling in the upper lobes signifies its presence. Miliary tuberculosis and silicosis may be confused by X-ray, although in the latter the nodules tend to coalesce.—*Radiographic Diagnosis in Diseases of the Lungs, J. G. Edwards, British M. J., September 14, 1935, no. 3897, 493.*—(*A. P.*)

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